PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	25 APR 2005
Applicant's or agent's file reference PU60525	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/32824	06 October 2004 (06.10.2004)	06 October 2003 (06.10.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/437; C07D 471/04; A61P 9/00 and US Cl.: 514/303; 546/118

Applicant

GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- [X] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [X] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [ ] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 2	YES
	Claims 1, 3-7	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-7	NO
Industrial applicability (IA)	Claims 1-7	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1, 3-7 lack novelty under PCT Article 33(2) as being anticipated by BAILEY et al. The Rho kinase inhibiting compounds described in the abstract, its composition and method of use, are encompassed by the instant claims wherein R1 is ethyl, cyclopropyl, or phenyl, X is O , S or NH, R2 is methyl or optionally substituted phenyl.

Claim 2 lack an inventive step under PCT Article 33(3) as being obvious over BAILEY et al. The Rho kinase inhibiting compounds described in the abstract with RN 607373-93-3 has an ethyl whereas the instant compound on page 122, lines 11-12 has a phenyl as R1. Ethyl and phenyl, however, are optional choices for R1 (corresponding to R2 in BAILEY et al). One of ordinary skill in the art would be motivated to replace the ethyl with the alternative phenyl to arrive at the instant invention.

Claim 2 meet the criteria set out in PCT Article 33(2), because the prior art does not specifically describe the compounds in the instant claim 2.

Claims 1-7 meet the criteria set out in PCT Article 33(4), and thus find industrial applicability because the subject matter claimed can be made or used in the pharmaceutical industry as a therapeutic agent for treating a disorder associated with inappropriate Rho kinase activity.